Atty. Dkt. No.: 3007E (071344-0305)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

#20
11/18/02

Applicant: Hein et al.

Title: TRANSGENIC PLANTS EXPRESSING ASSEMBLED SECRETORY ANTIBODIES

Appl. No.: 09/512,736

Filing Date: 02/24/00

Examiner: Collins, Cynthia E.

Art Unit: 1638

CERTIFICATE OF FACSIMILE TRANSMISSION

I hereby certify that this paper is being facsimile transmitted to the United States Patent and Trademark Office, Washington, D.C. on the date below.

Deborah Wykes

(Signature)

November 13, 2002

PETITION UNDER 37 C.F.R. § 1.182 to NULLIFY A TERMINAL DISCLAIMER

RECEIVED
FEB 06 2003
OFFICE OF PETITIONS

Commissioner for Patent
Washington, D.C. 20231

Sir:

This petition is filed to request nullification of a recorded terminal disclaimer in the pending case in accordance with MPEP § 1490A. Accompanying this petition is authorization to charge Deposit Account No. 50-0872 in the amount of $130.00 for the appropriate petition fee under 37 C.F.R. § 1.17(h) (fee code 1460).

Briefly, an obvious-type double patenting rejection was made over instant claims 53-66 for U.S. Patent Nos. 5,959,177, 5,639,947 and 5,202,422 in an Office Action dated November 11, 2001. Applicant filed a Terminal Disclaimer to remove the rejection on March 18, 2002. The Terminal Disclaimer was approved and the rejection withdrawn in an Office Action dated August 13, 2002.

This request to nullify the Terminal Disclaimer is based on amendments made to the claims that eliminate any purpose for having the Terminal Disclaimer. Prosecution to date has resulted in cancellation of claims 54, 55, 57-62, and 66. This leaves only claims 53, 56, and 63-65 remaining in the case that were subject to the rejection. Of these claims only claim 53 is

699

independent. Claim 53 as it existed at the time of the obvious-type double patenting rejection is shown below (see Preliminary Amendment of February 24, 2000).

> 53. A plant cell containing (a) nucleotide sequence encoding an immunoglobulin product containing at least a portion of an immunoglobulin light chain and (b) the immunoglobulin product encoded by said nucleotide sequences.

Instant claim 53 as presently amended is shown below.

> 53. (Amended three times) A plant cell containing:
>
> (a) nucleotide sequence encoding an immunoglobulin product comprising at least a portion of the variable region of an immunoglobulin light chain and a leader sequence forming a secretion signal, said light chain derived from an antigen-specific immunoglobulin comprising a heavy and light chain, and;
>
> (b) immunoglobulin product encoded by said nucleotide sequence wherein said leader sequence is cleaved from said immunoglobulin light chain following proteolytic processing, said light chain being capable of forming an antigen-specific immunoglobulin when co-expressed in a plant cell with said heavy chain from said antigen-specific immunoglobulin wherein said plant cell does not contain nucleotide sequence encoding said immunoglobulin heavy chain.

The difference between claim 53 as first filed versus as currently amended is shown below.

> 53. (Amended three times) A plant cell containing:
>
> (a) nucleotide sequence encoding an immunoglobulin product [containing] comprising at least a portion of the variable region of an immunoglobulin light chain and a leader sequence forming a secretion signal, said light chain derived from an antigen-specific immunoglobulin comprising a heavy and light chain, and;
>
> (b) immunoglobulin product encoded by said nucleotide [sequences] sequence wherein said leader sequence is cleaved from said immunoglobulin light chain following proteolytic

processing, said light chain being capable of forming an antigen-specific immunoglobulin when co-expressed in a plant cell with said heavy chain from said antigen-specific immunoglobulin wherein said plant cell does not contain nucleotide sequence encoding said immunoglobulin heavy chain.

It is readily apparent that substantial amendment has occurred following issuance of the obvious-type double patenting rejection. With this background established, Applicant will now address the propriety of the terminal disclaimer with respect to each referenced patent.

1. U.S. Patent Nos. 5,959,177

Claims 53-66 were rejected on November 11, 2001 under the judicially created doctrine of obviousness-type double patenting as being allegedly unpatentable over claims 6-12 of U.S. Patent No. 5,959,177. It was alleged that the conflicting claims were not patentably distinct because the transgenic plant comprising nucleotide sequences encoding immunoglobulin heavy and light chain polypeptides of U.S. Patent No. 5,959,177 would encompass the cells containing nucleotide sequences encoding the immunoglobulin products of claims 53-66 of the instant application.

Claims 6-12 of U.S. Patent No. 5,959,177 (the '177 patent) are directed to a transgenic plant containing nucleotide sequence encoding one or more immunoglobulin heavy-chain polypeptides. Claim 6 of the '177 patent is shown below.

6. A transgenic plant comprising:

a. plant cells that contain a nucleotide sequence encoding one or more immunoglobulin heavy-chain polypeptides, a nucleotide sequence encoding a polypeptide linker or joining chain, and a nucleotide sequence encoding a secretory component; and

b. immunologically active secretory antibodies encoded by said nucleotide sequences.

Notably, claims 6-12 of the '177 patent require the transgenic plant cells to include nucleotide sequence encoding a heavy chain immunoglobulin. This is in contrast to instant

claims 53, 56, and 63-65 which, as shown above, expressly exclude cells with such nucleotide sequence. Thus, there is no overlap between instant claims 53, 56, and 63-65 and claims 6-12 of the '177 patent. These two claim sets also should be separately patentable over the other for several reasons. First, a cell expressing the light chain alone is much different from a cell that expresses both a light and a heavy chain since the light chain is normally produced only in combination with a particular heavy chain which together form a heterodimer. In addition, at the time of the invention, antibodies were not known to be expressed by plants and there was a prejudice in the art against this possibility. This prejudice has been established by the Declaration of Richard Lerner, of record in the case. Lerner Declaration, ¶¶ 3-8.

> [T]here was a sound basis for a real prejudice in the art against using plants to produce a processed and assembled immunoglobulin which is antigen specific around the time of the During dissertation (*circa* 1988/1989). Were this not the case, then Applicant's invention clearly would not have been roundly hailed in both the scientific literature and in the general press as a significant scientific discovery and medical breakthrough.

Lerner declaration, ¶8 (footnotes removed).

Further supporting Applicant's position is the During Dissertation over which the claims have been rejected. As argued by Applicant, During attempted but failed to express an immunoglobulin light chain in plants which did not contain nucleotide sequence encoding a heavy chain. During's result suggests unique problems with achieving light chain expression when the heavy chain gene is absent from the cell, arguing for separate patentability of light chain expression alone versus expression of the immunoglobulin heterodimer.

Consistent with this view is the position taken by the Patent Office which issued a restriction requirement in this case on July 5, 2001 (made final an November 20, 2001). The restriction divided the claims into three groups: Group I: drawn to plant cells containing nucleic acid encoding both a heavy chain and light chain, Group II, drawn to plant cells containing nucleic acid encoding a heavy chain; and Group III, drawn to plant cells containing nucleic acid encoding a light chain. The rationale offered to support the restriction rested on the separate patentability of these three groups.

> The inventions are distinct, each from the other because of the following reasons: Inventions I and (II &III) are related as combination and subcombinations. Inventions of this relationship are distinct if it can be shown that (1) the combination as claimed does not require the particulars of the subcombination as claimed for patentability, and (2) that the subcombination has utility by itself or in other combinations (MPEP § 806.05(c)). In the instant case, the combination as claimed does not require the particulars of the subcombination as claimed because the combination recites 2 distinct subcombinations, the immunoglobulin heavy chain nucleotide sequence and the immunoglobulin light chain nucleotide sequence. Since both of these subcombinations is separately claimed, each serves as evidence that the other subcombination when combined is not the sole basis for patentability of the invention. The subcombination has separate utility such as for the production of heavy or light chain. Because these inventions are distinct for the reasons given above and the literature search required for one Group is not required for another Group, restriction for examination purposes as indicated is proper.

Thus, the position taken by the Patent Office to restrict the claims in this case is fully consistent with Applicant's arguments on behalf of this Petition to nullify the terminal disclaimer, (and is inconsistent with the original obviousness-type double patenting rejection). For all the above reasons, it is respectfully submitted that the Terminal Disclaimer is no longer necessary or appropriate for claims 6-12 of the '177 patent.

2. U.S. Patent Nos. 5,639,947

Claims 53-66 were rejected on November 11, 2001 under the judicially created doctrine of obviousness-type double patenting as being allegedly unpatentable over claims 1-7 of U.S. Patent No. 5,639,947. It was alleged that the conflicting claims were not patentably distinct because the transgenic plant comprising nucleotide sequences encoding immunoglobulin heavy and light chain polypeptides of U.S. Patent No. 5,639,947 would encompass the cells containing nucleotide sequences encoding the immunoglobulin products of claims 53-66 of the instant application.

Claims 1-7 of U.S. Patent No. 5,639,947 (the '947 patent) are directed to a transgenic plant containing nucleotide sequence encoding an immunoglobulin heavy and light chain polypeptides. Claim 1 of the '947 patent is shown below.

> 1. A transgenic plant comprising:
>
> (a) plant cells containing nucleotide sequences encoding immunoglobulin heavy- and light-chain polypeptides that each contain an immunoglobulin leader sequence forming a secretion signal; and
>
> (b) immunologically active immunoglobulin molecules encoded by said nucleotide sequences.

Notably, claims 1-7 of the '947 patent require the transgenic plant cells to include nucleotide sequence encoding a heavy chain immunoglobulin. This is in contrast to instant claims 53, 56, and 63-65 which, as shown above, expressly exclude cells with such nucleotide sequence. Thus, there is no overlap between instant claims 53, 56, and 63-65 and claims 1-7 of the '947 patent. Furthermore, these two claim sets also should be separately patentable over the other for same reasons as discussed above for claims 6-12 of the '177 patent. For all the above reasons, it is respectfully submitted that the Terminal Disclaimer is no longer necessary or appropriate for claims 1-7 of the '947 patent.

3. U.S. Patent Nos. 5,202,422

Claims 53-66 were rejected on November 11, 2001 under the judicially created doctrine of obviousness-type double patenting as being allegedly unpatentable over claims 1-3 of U.S. Patent No. 5,202,422. It was alleged that the conflicting claims were not patentably distinct because the plant cell composition and immunologically active glycosylated immunoglobulin of claims 1-3 of U.S. Patent No. 5,202,422 would encompass the cells containing nucleotide sequences encoding the immunoglobulin products of claims 53-66 of the instant application.

Claims 1-3 of U.S. Patent No. 5,202,422 (the '422 patent) are directed to a plant cell composition comprising a glycosylated immunoglobulin molecule free of sialic acid. Claim 1 of the '422 patent is shown below.

> 1. A composition comprising a glycopolypeptide multimer and plant material, wherein said multimer comprises an immunologically active glycosylated immunoglobulin molecule free of sialic acid residues

It is well known that an immunoglobulin molecule that is a multimer is a reference to an immunogloublin with at least a heavy chain variable region or immunologically active portion thereof and at least a light chain or immunologically active portion thereof containing heterodimer. Thus, common to claims 1-3 of the '422 patent is the requirement for a heavy chain immunoglobulin. This is in contrast to instant claims 53, 56, and 63-65 which, as shown above, expressly exclude cells with nucleotide sequence encoding a heavy chain immunoglobulin. Thus, there is no overlap between instant claims 53, 56, and 63-65 and claims 1-3 of the '422 patent. Furthermore, these two claim sets also should be separately patentable over the other for same reasons as discussed above for claims 6-12 of the '177 patent. For all the above reasons, it is respectfully submitted that the Terminal Disclaimer is no longer necessary or appropriate for claims 1-3 of the '422 patent.

It is believed that the Applicant has thoroughly explained why the Terminal Disclaimer is longer useful or appropriate for any of the listed patents. As suggested under MPEP §1490(A), relief is appropriate when, such as in this case, the Terminal Disclaimer does not take effect because the patent has not been granted and the public has not had the opportunity to rely on the Terminal Disclaimer. Thus, for all the above reasons, it is respectfully requested, that the Petition to nullify the Terminal Disclaimer be granted.

Atty. Dkt. No.: 300?E (071344-0305)

Respectfully submitted,

Date: November 11, 2002

By _____

Barry S. Wilson
Attorney for Applicant
Registration No. 39,431

FOLEY & LARDNER
Customer Number: 30542

30542
PATENT TRADEMARK OFFICE
Telephone: (858) 847-6722
Facsimile: (858) 792-6773